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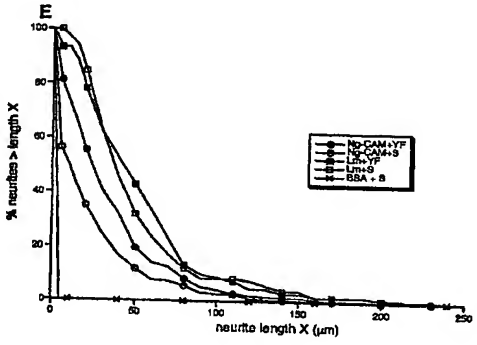
(54) Title: METHODS AND AGENTS FOR TREATING AXONAL DAMAGE, INHIBITION OF NEUROTRANSMITTER RELEASE AND PAIN TRANSMISSION, AND BLOCKING CALCIUM INFLUX IN NEURONS



(57) Abstract: The present invention pertains to methods to promote outgrowth of, or extension across a substrate of, neuronal cells by inhibiting the interaction between the cytoplasmic tail of the L1-CAM cell surface adhesion molecule and the cytoskeletal protein ankyrin. The invention also pertains to a method to treat diseases characterized by axonal damage such as spinal cord injury, traumatic brain injury, stroke, and neurodegenerative disease by administration of novel peptides that inhibit the binding of the L1-CAM cytoplasmic tail to ankyrin, and to pharmaceutical compositions comprising such peptides. The present invention pertains to the regulation of neuronal signal propagation. Addition of the peptide of the invention disrupts the interaction between the cytoplasmic tail of the cell surface adhesion molecule L1-CAM, the cytoskeletal protein ankyrin, and voltage-gated calcium channels at the presynaptic surface of a neuron leading to a transient redistribution of the calcium channels to cytoplasmic vesicles. This redistribution blocks signal propagation as demonstrated by the inhibition of voltage gated calcium current and a decreased secretion of Substance P, which mediates pain signaling. Furthermore, the invention pertains to a method of blocking calcium flux to protect against neural cell death following stroke or traumatic head injury.

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